Japanese Encephalitis Vaccine

“ Maintaining Support to Service Members”

Armed Forces Epidemiology Board
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By

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Problem Statement

- Current Mfg: BIKEN of Japan distributed through Aventis Pas
FDA licensure

- Current JE vaccine uses mouse brain derived cells for virus gr
known QC risks

- Japanese NRA requested a change to mfg methodology to allev

- BIKEN will close current mfg process in FY05 and move to in v
cell culture line.

- Gap in production until late FY06 for Japanese licensure
  US licensure will not start until after Japanese approval
  DoD funding necssary
  Best US licensure date FY09

Gap in production of 3-4 years

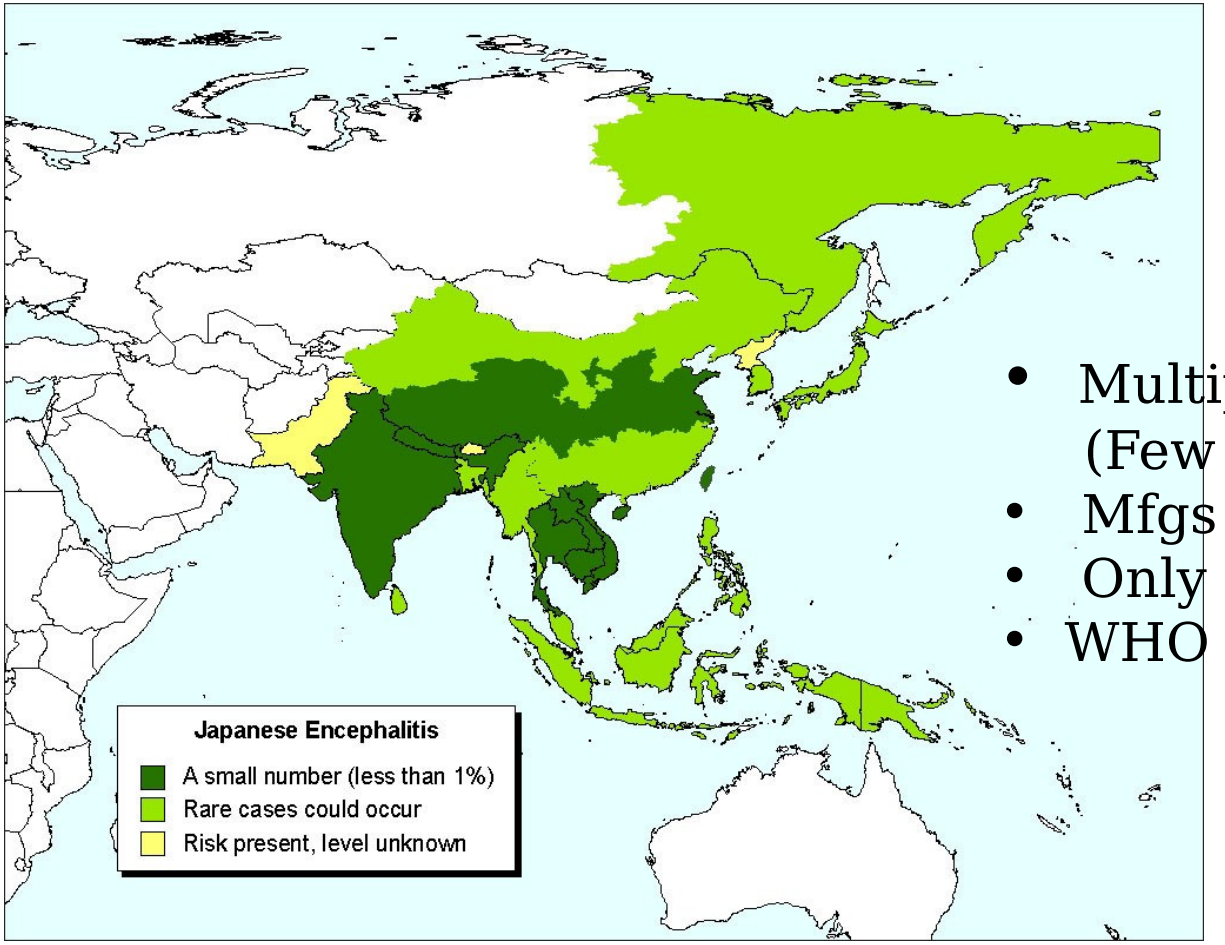
Operational Need

- PACOM & USF Korea maintain wartime contingency requirements (though unresourced at the moment)

- Approximately 90k doses purchased and used by services to
support Asian deployments (Navy and Marines predominantly)

- Disease Risk:
  - Mosquito borne vector
  - Largely within rural settings throughout East Asia
  - Would be a factor within wartime disruption and destruction of infrastructures
  - Attacks central nervous system causing disability and death

JE Vaccine MarketPlace



- Multiple technologies (Few FDA approvable)
- Mfgs thru-out Asia
- Only 1 US licensure
- WHO working toward a

Asia = 100s of mil doses/yr

US = 120k of dose/yr

JE Vaccine Future Sour

Three Manufacturers currently working on product that reach FDA approval

- Aventis Pasteur, using BIKEN product
- Intercell (Austrian Biotech) teamed w/VaccGen for
- Acambis

Conducted assessment of each firm's product and devel Timelines through a series of meetings at DSCP and foll Correspondence.

- DSCP for contracting and log mgmt
- WRAIR for vaccine development and technology
- MRMC for clinical and program mgmt
- DoD(HA) for policy and oversignt
- FDA for regulatory approval procedures

JE Vaccine Licensure Mo s

Non-Inferiority Study

Not much worse or not clinically inferior to a comparative agent

but never worse than placebo

Field Trial for efficacy not ethical nor practical (10 per 100,000 incidence rate)

Correlate of Protection can be used

- Historical data established serum plaque reduction neutralizing antibody as a surrogate marker
- Must establish a validated assay for test purposes
- Immunogenicity trial in the 200-300 range; safety in the 2-3000 range.

Overall Risk Assessm

Criteria	AP/BIKEN	Acambis	Intercell
Technology	Low	Med/low	Low
FDA Licensure	Low	Med	Low
Time to Approval	High	Med	Low
DoD Cost (Short term)	High	Low	Low
Mfg	Low	Med/low	Med/low
Log	Low	Low	Low

COA - Assumptions

- No shortfall of product is desired
- Rqmt stays consistent at 90k per year
- Contingency rqmts remain unresourced
- All additional costs are unprogrammed
- FDA allows 5 year shelf life of current product
- DSCP has procured additional 18 months of stockpile
- BIKEN closes production in FY05
- FDA will take longer than any mfg has on timeline
- US and European markets will stay small (under 1 mil
- Once new product is available, stockpile will become a
- DoD will ask FDA for fast track processing, to include r
- Additional stockpile brings financial risk to DSCP

Course Of Actions

#1: Sustain current production until an FDA appr available. Fund BIKEN toward US licensure as nec

Pros:

- Ensures no gap
- Provides means to cover contingency rqmts
- Unit cost of new product (BIKEN) least

Cons:

- Increased unit cost by at least 2x as of FY07 until final prod
- Could require up to $20 mil for clin trials & licensure

Bottom line: No risk approach but most expensiv and no program dollars have been POM'd

COAs

#2: Procure additional stockpile to cover thru FY0 BIKEN toward US licensure as necessary.

Pros:

- Ensures availability of product at min risk w/most secure m
- Provides means to build contingency rqmts under IND
- Cheapest unit price

Cons:

- Requires additional $13 mil in stockpile
- Could require up to $20 mil in Biken licensure costs

Bottom line: Assumes minor risk on product ava but still very expensive.

COAs

#3: Procure additional stockpile through FY08 and
stockpile for contingency since there will be no act
Do not Support any development/licensure. Monito

Pros:

- Provides reasonable coverage under a conservative estimat
- Provides for FDA approved contingency product vice IND p

Cons:

- Requires additional $8 (stockpile) + 5 (Contingency (100k d
- May require funds toward BIKEN if start-ups fail or fall to fa
- Long term sustainment costs would be higher

Bottom line: Assumes risk thru high confidence
achieving licensure, though on a more conservati
Adds contingency into mix. Accepts higher unit p

COAs

#4: Procure additional stockpile through FY08 an
Support any development/licensure. Monitor start

Pros:

- Provides reasonable coverage under a conservative estimat
- Production could be available under IND for contingency rq

Cons:

- Requires additional $8 mil in stockpile
- May require funds toward BIKEN if start-ups fail or fall to fa
- Long term sustainment costs would be higher

Bottom line: Assumes risk thru high confidence
achieving licensure, though on a more conservati
Accepts higher unit price

COAs

#5: Do nothing more and wait for industry

Pros:

- Requires no additional dollars at present

Cons:

- Start ups historically do not stay on time
- If additional stockpile needed, a one year lead time will occu

Bottom line: Assumes high risk that start-ups m

COAs

Recommendation: #3:
Procure additional stockpile through FY08
Procure small contingency (100k doses)
Do not support any development/licensure. Monit

Pros:

- Provides start-ups with a year of slippage
- Provides sufficient stockpile to start up BIKEN if start-ups fail
- Meets a limited contingency requirement

Cons:

- May result in extra product that would be financially eaten
- *Must find $13 mil in FY04/05*